EPInotes
Disease Prevention & Epidemiology Newsletter
SC Department of Health and Environmental Control

Vol. XXIII Issue No. 3 September - October 2002

Bioterrorism Update! Smallpox Pre-Event Planning for South Carolina

By Jerry Gibson, MD, MPH

This report summarizes the state of Pre-Event planning by DHEC and other partners to control spread of a possible smallpox case or cases in South Carolina. It includes the information distributed in recent video-conferences and emailed messages by the federal Department of Health and Human Services, including discussions and background papers on federal recommendations for who should be vaccinated, when, and with what conditions and exemptions, as well as estimates of the corresponding number of doses of vaccine that DHEC would be provided for us to deliver in this Phase 1 of the Pre-Event vaccination process. It is important to remember that: a) this article is based on statements by the Centers for Disease Control and other federal health agencies of their preliminary scientific assessments of how to do smallpox vaccination, adverse events and ways to minimize them, and educated speculations on what the Administration will eventually propose, and b) this summary discusses only what we will do to prepare **before** any smallpox event happened. Such preparation must include far more than simply vaccinating a specific set of South Carolina first-response personnel; it must also include preparations for rapidly identifying and reporting the first case(s), training and planning for immediate outbreak investigation and containment of further spread of infection, and assuring we can give effective clinical care and isolation to those cases, even if they are in substantial numbers.

Background: The perception of a need to prepare for a possible smallpox attack is based on the following facts: Smallpox is only **moderately** communicable as an infectious disease, but it has severe and dramatic symptoms with a case-fatality of about 30%. Although it was eradicated in 1976 (and by 1950 in the US), the former Soviet bioweapons program succeeded in weaponizing smallpox in the 1980s, and produced tons of virus, much still unaccounted for. There is good evidence that Soviet experts using the weaponized form of smallpox virus were able to disseminate it by the airborne route, but this probably required sophisticated technology and it is not known whether governments in Iraq or North Korea would have the technical skill to do this. However, several nations have shown strong interest in acquiring bio-weapons such as smallpox, and probably have access to the virus. The probability of an actual smallpox biological attack on

see Bioterrorism Update on page 2

West Nile Virus Update: Clinical Presentation, Diagnosis and Reporting

By K. Mills McNeill, MD, PhD, Art Wozniak, DrPH

With the identification of West Nile virus (WNV) in South Carolina, WNV infection should be considered in persons of all ages who present with unexplained encephalitis or meningitis. Recent information from the Centers for Disease Control and Prevention (CDC) is summarized, and laboratory diagnostic services provided by SCDHEC Bureau of Laboratories (BOL) are described.

Clinical Features of Human WNV Infections in the U.S.

- **Mild Illness**. Most WNV infections are mild and often clinically inapparent. About 20% of those infected will develop a mild illness without neurological signs (West Nile fever). The incubation period is thought to range from 3 to 14 days, and symptoms generally last 3 to 6 days. Reports from earlier outbreaks describe the mild form of WNV infection as a febrile illness of sudden onset often accompanied by malaise, headache, anorexia, myalgia, nausea, vomiting, rash, lymphadenopathy and eye pain. The full clinical spectrum of WN fever has not been determined in the U.S.
- **Severe Illness**. Severe neurological disease occurs in approximately 1 in 150 infected persons. The most significant risk factor for developing severe neurological disease is advanced age. Encephalitis is more commonly reported than meningitis. In recent outbreaks, symptoms occurring among patients hospitalized with severe disease included fever, weakness, GI symptoms, and change in mental status. A minority of patients with severe disease developed a maculopapular or morbilliform rash involving the neck, trunk, arms, or legs. Several patients experienced severe muscle weakness and flaccid paralysis.

see West Nile Virus Update on page 3

INSIDE THIS ISSUE

(Bioterrorism Update - continued from page 1)

the United States cannot be estimated.

But there are several pieces of good news too:

a) The vaccine is very easy to administer, and is essentially 100% protective for 5-10 years in patients with a good "take". During the smallpox eradication program in the Indian subcontinent and Africa, health officers (including American epidemiologic officers from the CDC) diagnosing and giving clinical care for smallpox cases were protected only by being well vaccinated, and never used or needed respiratory or other forms of personal protection against infection in order to remain uninfected. Furthermore, vaccination of a contact within 3-4 days after significant exposure to a case will either protect against getting the disease, or result in non-fatal "modified" disease.

b) Smallpox is transmitted over 85% of the time by the "droplet contact" route, which requires face-to-face direct contact within 6 feet of a case. At most 5-10% of cases are "flat" or "hemorrhagic" forms of the disease that sometimes are more infectious and can transmit the virus by the true airborne route (i.e. to persons more than 6 feet away.) These epidemiologic observations are validated by the fact that smallpox was eradicated successfully using only the "surveillance and containment" method, in which cases, and also face-to-face contacts of cases, are isolated and contacts are vaccinated, so that they cannot spread the disease further. Then "rings" of persons living around each cases are successively vaccinated to prevent the virus from spreading. But the approach of simply trying to vaccinate the entire population in which cases were occurring (mass vaccination) was a failure; the surveillance and containment strategy was developed because mass vaccination consistently did not work. Effective smallpox control seems to require focusing isolation and vaccination efforts on the high-risk persons surrounding cases. Mass vaccination of the local population may be done in addition.

c) This strategy worked partly because about 85%+ of smallpox cases have a very characteristic pustular rash and are easy to detect and to diagnose, once the clinician knows what it looks like. That is why CDC and DHEC are distributing thousands of the "Evaluating Patients for Smallpox" posters to health care personnel. The "flat" and hemorrhagic clinical presentations mentioned above are much harder to diagnose clinically, and such a case might be misdiagnosed as meningococcemia (for example) for several days.

d) The vaccine has a low incidence of **severe** side effects ("Adverse Events" or AEs), seen primarily in primary vaccinations and in people with underlying disease of two types: abnormal T-cell mediated immune function, and a history of certain skin diseases such as eczema and atopic dermatitis. Based on data from the US vaccination program in the 1960s, from every million people vaccinated about 1-2 persons would die and about 15 would get life-threatening cases of encephalitis or eczema vaccinatum. Also somewhere between 15-30% would have severe enough fever, malaise and local tenderness (resembling a bacterial cellulites but caused by the virus) to miss one or more days of work. Vaccinated persons occasionally inadvertently transmitted the virus to other persons, but the great majority of those events were from one small child to another and this rarely happened in a healthcare work setting.

Based on these disease characteristics, our Pre-Event Smallpox Preparation Plan is very likely to have the following characteristics:

1. The Initial Phase will consist of rapid training of DHEC personnel to form a number of Smallpox Vaccination and Outbreak Response Teams, who will then proceed to offer vaccination to volunteers in all South Carolina acute care hospitals that could safely contain a smallpox case. These volunteer hospital employees would be chosen by the hospital and would be staff responsible for two basic tasks in their hospital: a) Providing clinical care to smallpox cases who presented to their hospital, and b) Serving in the emergency or other departments where they might be the first to encounter the initial smallpox case(s). Such vaccination of hospital employees would begin around 60 days after DHEC is given the "go-ahead" by the federal Secretary for Health and Human Services. This is likely to be a total of around 7000-8000 persons in South Carolina. We can predict some of the conditions required for such vaccinations: a) Job furloughs will **not** be required, but vaccinated personnel will be required to wear an occlusive dressing on the vaccination site while at work and to have it changed regularly; b) The vaccine may be FDA-approved, so that special research informed consents would not be necessary and workman's compensation and (usually) personal health insurance would cover the vaccinated staff; c) Vaccination volunteers will be carefully informed and screened for contraindications, and offered pregnancy and HIV tests.

2. The Second Phase would begin in 2003, during which vaccination would be offered to a wider pool of first responders to a smallpox incident. These would probably include other primary health care providers, emergency medical technicians, and law enforcement officers.

3. The Third Phase is more controversial. If it happens, it would include offering the vaccine to all other residents of the United States excluding infants. The same rigorous screening for immune deficiencies and eczematous skin disease would be done.

By the time this article is published, it is likely that the final federal HHS recommendation and "go-ahead" will have happened. It is not likely to be very different than the above. ✍

(West Nile Virus Update - continued from page 1)

Neurological presentations included ataxia and extrapyramidal signs, cranial nerve abnormalities, myelitis, optic neuritis, polyradiculitis, and seizures. Although not observed in recent outbreaks, myocarditis, pancreatitis, and fulminant hepatitis have been described.

Routine Laboratory and Radiographic Test Results

Patients in recent outbreaks have demonstrated the following laboratory and radiographic results:

- Total leukocyte counts in peripheral blood were mostly normal or elevated, although lymphocytopenia and anemia have been seen.
- Hyponatremia may be present, particularly among patients with encephalitis.
- CSF examination reveals a pleocytosis, usually with a predominance of lymphocytes, elevated protein, and normal glucose.
- CT scans of the brain generally have revealed no evidence of acute disease; in about 1/3 of patients, MRI has revealed enhancement of the leptomeninges, the periventricular areas, or both.

Laboratory Diagnostic Testing for West Nile Virus

The SCDHEC BOL offers tests for WNV antigen and WNV-specific antibody in selected patients upon physician request. Because of strict limitations on reagents, this testing will be prioritized for hospitalized patients with viral encephalitis and meningitis. The turn-around time will vary depending upon the test(s) requested (see below). Since priority must be maintained for other essential public health laboratory procedures not available elsewhere, e.g., rabies testing, the use of commercial laboratories should be considered in those instances in which a short turnaround time for WNV results is critical for the clinical management of an individual patient.

- **Tests for virus antigen in cerebrospinal fluid (CSF)**. CSF specimens collected **LESS THAN 10 days after onset of symptoms** may be tested for WN virus antigen by PCR. Currently, these are run daily (M-F); therefore, negative results will usually be reported within 1 working day of receipt of the specimen. If the PCR is positive, an additional 2-3 days will be required for confirmation.
- **Tests for IgM and IgG antibody in CSF and serum**.
  - **IgM antibodies** can be detected by enzyme immunoassay (EIA) in CSF and serum during the acute phase of WNV infection. According to the CDC, most patients will demonstrate IgM antibodies in CSF and serum within 8 days after onset of symptoms. Specimens submitted less than 8 days after onset of symptoms that test negative should be interpreted as indeterminate for WNV; therefore, these patients may require retesting at a later date. For this reason, IgM testing of specimens collected earlier than 8 days after onset of symptoms is not routinely recommended.
  - **An IgG antibody titer rise** can be detected by EIA in acute (collected within 7 days of illness onset) and convalescent (collected 14-21 days after illness onset) sera in WNV patients.

NOTE: Since WNV EIA's are performed on a weekly basis at BOL, **negative** serological results will generally be reported 1-2 weeks after receipt of the serum specimen. All **positive** EIA's require confirmation by plaque reduction neutralization testing (PRNT) at the CDC. Therefore, up to 2 weeks or more additional time will be required to report positive serological results.

Requesting Laboratory Diagnostic Support from SCDHEC

Physicians may contact the Division of Acute Disease Epidemiology at 803-898-0861 (pager 803-690-3756 after hours and on weekends) to telephonically report suspect cases of WNV and to request laboratory testing by SCDHEC. If the patient meets the strict clinical criteria described above, authorization will be given for WNV testing. The physical address for shipment of specimens is: SCDHEC Bureau of Laboratories, ATTN: Virology Laboratory, 8231 Parklane Road, Columbia, SC 29223, Tel. 803-896-0819. Cerebrospinal fluid specimens shipped within 24-48 hours of collection may be sent on cold pack; CSF specimens held for longer periods prior to shipment should be frozen. Serum may be shipped at room temperature. Commercial overnight carrier is recommended for all shipments. Physicians remain free to offer their patients WNV testing through commercial laboratories if this testing cannot be provided by SCDHEC.

Treatment

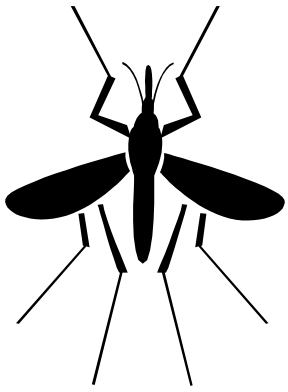
Treatment is supportive and often involves hospitalization, administration of intravenous fluids, respiratory support, and prevention of secondary infections in patients with severe disease. Ribavirin in high doses and interferon alpha-2b have some activity against WNV *in vitro*.

However, no controlled studies have been completed on the use of these or other medications, including steroids, antiseizure drugs, or osmotic agents, in the management of WNV encephalitis.

References

1. CDC. West Nile Virus (WNV) Infection: A Primer for the Clinician. Available at <www.cdc.gov/ncidod/dvbid/westnile/resources/fact_sheet_clinician.htm>

2. Peterson LR, Marfin AA. West Nile virus: A primer for the clinician. Ann Int Med 137(3), 173-179, 2002. Available at <www.acponline.org>



Laboratory Survey of Antiboiotic Nonsusceptibility among *Streptococcus pneumoniae* Isolates in South Carolina, 1998 vs. 2000

By Jerry Gibson, MD, MPH

Community-acquired infections with drug-resistant *S. pneumoniae* (DRSP) have emerged as a major public health concern in the United States (1-3). The emergence of DRSP underscores the need for timely, local, population-based surveillance of antibiotic resistance. In 1998, the South Carolina Department of Health and Environmental Control (DHEC) surveyed clinical microbiology laboratories statewide to determine the extent of screening and antimicrobial susceptibility testing of *S. pneumoniae* and the prevalence of penicillin nonsusceptibility (PCN-N) and extended-spectrum cephalosporin nonsusceptibility (ESC-N). The 1998 study reviewed data from January 1, 1998 through September 30, 1998.

This article summarizes the results of the follow-up study conducted in 2001 and compares the results with data from the 1998 study. The 2001 survey results will aid in identifying time and geographic trends in resistance rates, as well as in creating guidelines for empiric therapy for practitioners in South Carolina.

In 2001, DHEC used an updated version of the 1998 standardized questionnaire that was expanded to include questions pertaining to levofloxacin nonsusceptibility (LEV-N). A survey was mailed to 89 clinical microbiology laboratories.

Sixty-one (68.5%) of the 89 clinical microbiology laboratories surveyed responded. Thirty-four (73.9%) of the 46 counties in South Carolina were represented in the study.

Statewide Prevalence

Statewide prevalences of PCN-N, ESC-N, and LEV-N were calculated using the MIC test result data reported by the laboratories. The prevalence of PCN-N was 38.4%, with 20.9% of isolates intermediately resistant and 17.5% high-level resistant. The prevalence of PCN-N was higher in 2000 than in 1998 (34.5%, Chisquare p=0.01).

The prevalence of ESC-N among pneumococcal isolates was 17.7%, with 11.7% of isolates intermediately resistant and 6.0% high-level resistant. Although the prevalence of ESC-N decreased from 1998 (19.1%), the difference was not significant (Chi-square p=0.25).

The prevalence of LEV-N among pneumococcal isolates was 0.8%, with 0.5% of isolates intermediately resistant and 0.3% high-level resistant.

Prevalence by Public Health District

It was possible to calculate PCN-N and ESC-N prevalence data for 11 of DHEC's 13 health districts. For health district PCN-N prevalence calculations, the sample size of isolates ranged between 17 and 562, and the median sample size of isolates was 106.

This study indicates a high prevalence of PCN-N (38.4%), ESC-N (17.7%) and LEV-N (0.8%) among *S. pneumoniae* isolates in South Carolina in 2000. These results are similar to or higher than recent CDC pneumococcal surveillance system data. The CDC's Active Bacterial Core Surveillance (ABCs), which includes 8 states (California, Connecticut, Georgia, Maryland, Minnesota, New York, Oregon, and Tennessee), reported the following prevalences in 2000: PCN-N, 27.4%; cefotaxime nonsusceptibility, 17.8%; and LEV-N, 0.3% (4).

The prevalence of PCN-N, ESC-N, and LEV-N does not appear to be geographically uniform in South Carolina. Both the prevalence of PCN-N (range 21.7%-64.7%) and ESC-N (range 8.5%-30.6%) varied greatly among health districts. The geographic variation in the prevalence of PCN-N and ESC-N found in this study emphasizes the importance of community-based surveillance of pneumococcal susceptibility to antibiotics.

Because penicillin susceptibility cannot be assumed, all pneumococcal isolates associated with disease should be screened routinely for penicillin susceptibility by disk diffusion using a 1µg oxacillin disk, which is highly sensitive for PCN-N. This study indicated that only 42.6% of responding clinical microbiology laboratories in South Carolina screen pneumococcal isolates with an oxacillin disk for penicillin nonsusceptibility.

The prevalence estimates provided are sufficient to guide healthcare providers in selecting appropriate empiric therapy for suspected pneumococcal infections. Due to the high rates of resistance, South Carolina healthcare providers should consider the possibility of PCN-N, ESC-N, and LEV-N when treating suspected *S. pneumoniae* infections (3).

Present intervention strategies have yet to identify how much reduction is necessary in antimicrobial usage to reverse the increase in antibiotic resistance, or whether a reduction in pneumococcal resistance is achievable. However, prevalence data permits improved prescribing representing the patient's best interest. A number of prevention strategies should be promoted to decrease infections with DRSP in South Carolina, including adherence to the Advisory Committee for Immunization Practices recommendations regarding use of the 23-valent pneumococcal polysaccharide vaccine for persons 2 years of age or older with increased risk for pneumococcal disease (5), use of Prevnar™, the 7-valent pneumococcal conjugate vaccine, among children less than 2 years of age, and continuation of the statewide Careful Antibiotic Use Program.

References

1. Duchin JS, Breiman RF, Diamond A, et al: High prevalence of multidrug-resistant *Streptococcus pneumoniae* among children in a rural Kentucky community. *Pediatr Infect Dis* 1995; 14 (9):745-750
2. Breiman RF, Butler JC, Tenover FC, et al: Emergence of drug-resistant pneumococcal infections in the United States. *JAMA* 1994; 271:1831-1835

see Laboratory Survey on page 5

(Laboratory Survey - continued from page 4)

3. Dowell SF, Butler JC, Giebink GS, et al: Acute otitis media: management and surveillance in an era of pneumococcal resistance-a report from the Drug-resistant Streptococcus pneumoniae Therapeutic Working Group. *Pediatr Infect Dis* 1999; 18:1-9
4. Centers for Disease Control and Prevention: Active Bacterial Core Surveillance (ABCs) Report, Emerging Infections Program Network, Streptococcus pneumoniae, 2000. *http://www.cdc.gov/ncidod/dbmd/abcs/survreports/spneu00.pdf*, 2001
5. Heffernan R, Henning K, Labowitz A, et al: Laboratory survey of drug-resistant *Streptococcus pneumoniae* in New York City, 1993-1995. *Emerg Infect Dis* 1998; 4:113-116 ✍

Hepatitis Hints
By Robert Ball, MD, MPH

Hepatitis C should be diagnosed first by a screening test for antibody (most commonly done by the EIA method). If positive, a confirmatory test should be ordered. The clinician may choose either the RIBA antibody test or the RNA PCR. The RIBA antibody test verifies if the EIA antibody results reflect true antibodies to hepatitis C virus or a cross-reacting non-specific antibody. The PCR - whether qualitatitive or quantitative - detects the presence of the virus by direct measurement. However, a person can have HCV infection and, on rare occasions, the PCR may be below limit of detection (ie, "negative"). Hence, if the RIBA is performed and is positive, then the PCR should be done to detect if HCV is still present or if the patient is one of those 15-20% who spontaneously resolves. If the PCR is done and is negative, a RIBA should be done. If the RIBA is positive, then the PCR should be repeated once. ✍

Hepatitis C in South Carolina: An Update
By Robert Ball, MD, MPH

DHEC Bureau of Disease Control (BDC) medical epidemiologists estimate that South Carolina has an estimated 50,000-70,000 persons infected with hepatitis C (as extrapolated from very good CDC national survey data). The CDC estimates that there are at least 3-4 million Americans with chronic hepatitis C, many more than the estimated 1 million with HIV-AIDS. Hepatitis C is transmitted similarly to HIV, namely by exchange of blood and genital fluids via needle-sharing, transfusions (prior to screening mid-1992), sex, and perinatally. Hepatitis C prevention methods parallel those in HIV programs. Hepatitis C is the most common bloodborne pathogen in the USA and is now the leading cause of chronic liver disease (more than alcohol) and the leading medical indication for liver transplantation. Surgeon-General Dr. David Satcher called hepatitis C "The Silent Epidemic". Although many persons with chronic hepatitis C seem stable for 1-2 decades, at least 1/4 to 1/3 progress to chronic liver disease, cirrhosis, and premature death. The USA's costs for direct medical care (including liver transplantation) were estimated to have exceeded $ 5-10 billion in 2000, exceeding HIV-AIDS costs and representing a major and increasing economic burden for our population.

DHEC BDC has long had surveillance systems for acute (incident) communicable diseases including hepatitis C and also has a Chronic Viral Hepatitis Surveillance Registry, which through June 2002 contained 11,243 reported cases. Unfortunately, most citizens with chronic hepatitis C do not know they are infected, and those who do know are often unsure what to do about their infection. Similarly, the medical profession is still learning about hepatitis C.

Similar to HIV, there are relatively simple serologic tests for hepatitis C (see "Hepatitis Hints" in this issue) that can diagnose a person with hepatitis C. Further testing can assist specialists in determining if the person is a candidate for therapy. Currently approved therapies, given to appropriate treatment candidates for 6-12 months, cure at least 2-3 of every 5 patients completing therapy. An economic report indicated a 4:1 Return on Investment if patients are treated early rather than wait until complications develop. A recent medical report (New England Journal of Medicine 11-15-02) indicated that if detected early (within the first half-year), hepatitis C can be cured with 6 months of single-drug Interferon therapy in 98% of patients.

Identification of infected persons can assist them in preventing further liver damage (ie, avoid alcohol), prevent transmission to others by appropriate counseling, and provide referral access to medical evaluation for consideration of therapy. Hence identifying and treating persons with hepatitis C early will save both lives and resources. At 5 county health departments in SC (Spartanburg, Charleston, Greenwood, Walterboro, and Florence), DHEC is now offering hepatitis C risk assessment, counseling and free testing, referral, and partner notification within the context of existing HIV and STD programs. The SC Hepatitis C Coalition (supported in part by DHEC) provides awareness and support services, an annual conference (Thursday November 14 in Columbia) and a statewide physician referral list. Their phone number is 803-898-9562; their website is http://www.ahec.net/HepatitisC. ✍

Rabies Exposure!
What Would You Do?
By Robert T. Ball, Jr., MD, MPH

Question: While asleep, your patient is bitten on the fingertip at night, presumably by a rat or mouse, which have been seen in the house. Should postexposure prophylaxis be administered?

Answer: Rabies prophylaxis in the setting of exposures to small mammals, including rodents, lagomorphs (rabbits and hares), and insectivores (e.g., shrews), is almost never required. These animals are not reservoirs and there have been no documented cases of rabies transmission to humans by these animals. On rare occasions, squirrels have been found rabid, and rabies PEP may be considered for their bite victims. If there is any question, you should call your local or state health department physician consultant. ✍

Epi-Notes
Division of Acute Disease Epidemiology
SC DHEC
2600 Bull Street
Columbia, SC 29201

Return Service Requested

Epi-Notes is published by the South Carolina Department of Health and Environmental Control - Division of Acute Disease Epidemiology
FOR DISEASE REPORTING

Urgently reportable condiditons must be phoned to the local county health departments or Division of Acute Disease Epidemiology within 24 hours of diagnosis. On nights and weekends, call 888-847-0902 and ask to have the person in your county responsible for disease reporting paged.

For a copy of the current Official List of Reportable Conditions, call 803-898-0861 or visit www.scdhec.net/hs/diseasecont/disease.htm.

For disease consultation or additional reporting, telephone (803) 898-0861 during normal working hours (Monday-Friday, 8:30 am - 5:00 pm EST).

Non-urgent conditions can be reported by calling your local county health department or by mailing a completed DHEC DISEASE REPORTING CARD (DHEC 1129) to the county health department.

South Carolina Department of Health and Environmental Control